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Appl. No. 10/556,901
Atty. Dkt.: 620-401
Amendment After Final Rejection
March 20, 2008

REMARKS

Reconsideration is requested.

Claims 1-4, 6-9, 11-20, 22-29, 31, 34-39, 41-48 and 50 are pending. Claims 1-4, 6-9, 11-20 and 22-29 have been withdrawn from consideration.

Claims 13-20, 22-29, 35-36, 41-43 and 50 have been canceled above, without prejudice. Claims 1-9, 11 and 12 have been revised above to be dependent from compound claims 34, 37-39, and 44-48, respectively, to place the claims in condition for rejoinder and allowance with the compound claims. Entry of the present Amendment and rejoinder and allowance of the dependent method claims with the amended compound and composition claims are requested. No new matter has been added.

The Section 112, second paragraph, rejection of claim 34 is traversed. The term solvate, as claimed, is well known to those of ordinary skill in the art and the metes and bounds of same will be appreciated by one of ordinary skill in the art.

A search of the U.S. Patent Office on-line records reveals that 3,292 U.S. patents have issued since 1976 with claims containing the term "solvate". The following is a listing of the first 50 "hits" of the U.S. Patent Office search.

PAT.	Title
NO.	
1	<u>7,345,175</u> T <u>Biphenyl derivatives</u>
2	<u>7,345,093</u> T <u>Methods of enhancing solubility of compounds</u>
3	<u>7,345,087</u> T <u>Aminocyclohexyl ether compounds and uses thereof</u>
4	<u>7,345,086</u> T <u>Uses of ion channel modulating compounds</u>
5	<u>7,345,085</u> T <u>Indoles having anti-diabetic activity</u>
6	<u>7,345,060</u> T <u>Compounds having .beta..sub.2 adrenergic receptor agonist and muscarinic receptor antagonist activity</u>
7	<u>7,345,059</u> T <u>Diphenylpyridine derivatives, preparation and therapeutic application thereof</u>

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- 8 7,345,057 T 5-HT7 receptor antagonists
- 9 7,345,038 T Pyridyloxymethyl and benzisoxazole azabicyclic derivatives
- 10 7,345,033 T Carbamoyl-and thiocarbamoyl-phosphonates and pharmaceutical compositions comprising them
- 11 7,344,733 T Matrix controlled transdermal therapeutic system for the use of pramipexole and ropinirole
- 12 7,342,131 T Levodopa prodrugs, and compositions and uses thereof
- 13 7,342,041 T 3,4-(cyclopentyl)-fused proline compounds as inhibitors of hepatitis C virus NS3 serine protease
- 14 7,342,016 T Farnesyl protein transferase inhibitors as antitumor agents
- 15 7,342,013 T Benzamides and related inhibitors of factor Xa
- 16 7,341,709 T Compositions for labeling beta.-amyloid plaques and neurofibrillary tangles
- 17 7,339,079 T Thyronamine derivatives and analogs and methods of use thereof
- 18 7,339,065 T Design and synthesis of optimized ligands for PPAR
- 19 7,339,060 T Preparation of cabergoline
- 20 7,338,976 T Heterocyclic esters or amides for vision and memory disorders
- 21 7,338,951 T Pyridine compounds
- 22 7,335,799 T Hydroxyl compounds and compositions for cholesterol management and related uses
- 23 7,335,689 T Dihydroxyl compounds and compositions for cholesterol management and related uses
- 24 7,335,670 T Derivatives of N-[heteroaryl(piperidine-2-yl) methyl]benzamide, preparation method thereof and application of same in therapeutics
- 25 7,335,649 T Thrombopoietin mimetics
- 26 7,335,648 T Non-nucleotide composition and method for inhibiting platelet aggregation
- 27 7,332,606 T Process for producing 1-benzyl-4-[5,6-dimethoxy-1-indanon]-2-ylmethylpiperidine or hydrochloride thereof
- 28 7,332,492 T Amino substituted dibenzothiophene derivatives for the treatment of disorders mediated by NP Y5 receptor
- 29 7,332,484 T 2,4-pyrimidinediamine compounds and their uses
- 30 7,332,481 T Thrombopoietin mimetics
- 31 7,329,752 T Carbamate compounds as 5-HT_{sub}4 receptor agonists
- 32 7,329,749 T Piperazinylcarbonylquinolines and -isoquinolines
- 33 7,329,685 T 1-Phenyl-2-oxo-3-sulfonylamino-pyrrolidine derivatives and related compounds as factor Xa inhibitors for the treatment of acute vascular diseases
- 34 7,329,684 T Benzimidazole derivatives as therapeutic agents
- 35 7,329,672 T 2,4-pyrimidinediamine compounds and their uses
- 36 7,329,671 T 2,4-pyrimidinediamine compounds and their uses

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37 7,329,655 T Nitrogenous heterocyclic compounds
38 7,329,318 T Methods of crystal precipitation
39 7,326,792 T Heterocyclic compounds as P2X7 ion channel blockers
40 7,326,790 T Diphenylioxazole compounds and hydro isomers thereof
41 7,326,788 T Quinolinone derivatives as inhibitors of c-fms kinase
42 7,326,732 T EP2 receptor agonists
43 7,326,729 T CXCR1 and CXCR2 chemokine antagonists
44 7,326,723 T Aralkyl-tetrahydro-pyridines, their preparation and pharmaceutical compositions containing same
45 7,326,720 T Phenyl- and pyridylpiperidines with TNF activity
46 7,326,690 T Modulation of cell fates and activities by phthalazinediones
47 7,323,585 T Levodopa prodrugs, and compositions and uses thereof
48 7,323,537 T Catalyst for production of polyester, process for producing polyester using it and titanium-containing polyethylene terephthalate
49 7,323,496 T Compounds for treatment of inflammation, diabetes and related disorders
50 7,323,494 T Compounds and methods

While the applicants have not review all of the listed patents, the claims of the first 10 listed patents at least contain a reference to "solvate" in a manner recited in the present claims, without the further recitation required by the present Examiner.

Of the patents identified in the above-described search, 74 patents were identified which include the word "solvate" in the claims and were granted by the Primary Examiner, Examiner Seaman, who signed the Office Actions of December 21, 2007 and August 23, 2007. The following list of 50 patents are the most recent of these 74 patents identified:

- 1 7,326,788 T Quinolinone derivatives as inhibitors of c-fms kinase
- 2 7,320,990 T Crystalline form of a biphenyl compound
- 3 7,317,102 T Diarylmethyl and related compounds
- 4 7,317,022 T Benzimidazolone-carboxamide compounds as 5-HT_{sub}4 receptors agonists
- 5 7,314,937 T Non-imidazole aryl alkylamines compounds as histamine H3 receptor antagonists, preparation and therapeutic uscs

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- 6 7,288,657 T Biphenyl compounds useful as muscarinic receptor antagonists
- 7 7,288,543 T Opioid receptor antagonists
- 8 7,256,293 T Imidazopyridine intermediates
- 9 7,241,907 T Acetone solvate of dimethoxy docetaxel and its process of preparation
- 10 7,230,108 T Quinoline derivatives as glucokinase ligands
- 11 7,223,776 T Compounds with anti-bacterial activity
- 12 7,214,798 T Derivatives of piperidinyl-and piperazinyl-alkyl carbamates, preparation methods thereof and application of same in therapeutics
- 13 7,202,271 T Fused pentacyclic polyethers
- 14 7,192,968 T Ethylenediamine derivatives
- 15 7,189,736 T Prodrugs of imidazopyridine derivatives
- 16 7,183,414 T Processes for the preparation of benzimidazole derivatives
- 17 7,183,411 T Naphthol, quinoline and isoquinoline-derived urea modulators of vanilloid VR1 receptor
- 18 7,179,920 T 3-thia-4-arylquinolin-2-one derivatives
- 19 7,176,220 T 4-oxoquinoline compound and use thereof as pharmaceutical agent
- 20 7,176,213 T Imidazoquinoline derivatives and their use as adenosine A3 ligands
- 21 7,151,180 T Potassium channel modulators
- 22 7,145,013 T 3-thia-4-arylquinolin-2-one derivatives
- 23 7,141,671 T Biphenyl derivatives
- 24 7,132,542 T Compounds for the treatment of male erectile dysfunction
- 25 7,098,340 T Benzyl sulfonamide derivatives
- 26 7,087,758 T Quinoline inhibitors of hyaki and hyak3 kinases
- 27 7,087,749 T Substituted piperidine compounds and methods of their use
- 28 7,067,530 T Compounds, their preparation and use
- 29 7,064,207 T Androgen receptor antagonists
- 30 7,060,712 T Crystalline form of aryl aniline .beta..sub.2 adrenergic receptor agonist
- 31 7,057,048 T Androgen receptor antagonists
- 32 7,037,925 T 4-anilinoquinolin-3-carboxamides
- 33 7,030,246 T Tetrahydroquinoline derivatives as stat6-modulators, preparation and use thereof
- 34 7,030,145 T Pyridinyl derivatives for the treatment of depression
- 35 7,009,052 T Sulfonamide derivatives
- 36 6,995,174 T Hepatitis C virus inhibitors
- 37 6,977,266 T Pyridone derivatives having affinity for cannabinoid 2-type receptor
- 38 6,949,656 T Cyclic amine derivatives and use thereof
- 39 6,939,968 T Atropisomers of 3-substituted-4-arylquinolin-2-one derivatives
- 40 6,906,090 T Compositions and methods for treating mycobacterial diseases

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- 41 6,903,215 T Glucocorticoid mimetics, methods of making them, pharmaceutical compositions, and uscs thereof
- 42 6,870,055 T Isoquinolinone potassium channels inhibitors
- 43 6,852,734 T Indole derivatives exhibiting chymase-inhibitory activities and process for preparation thereof
- 44 6,844,357 T Substituted quinolin-2-one derivatives useful as antiproliferative agents
- 45 6,841,560 T Substituted isoquinoline derivatives and their use as anticonvulsants
- 46 6,815,465 T Heterocyclic compounds inhibiting angiogenesis
- 47 6,800,643 T Mixtures for organic compounds for the treatment of airway diseases
- 48 6,770,661 T Aryl substituted pyridines and their use
- 49 6,756,370 T Piperidine alcohols
- 50 6,713,645 T Substituted tricyclics

The results of the U.S. Patent Office search is evidence that the rejected recitation of the present claims is well understood by those of ordinary skill in the art. The applicants respectfully disagree with the Examiner's assertion that "What is allowed in the issued US patent data base is of no consequence to prosecution at hand." In fact, the terms and phrases of allowed U.S. patents in the chemical arts evidence a recognized understanding in the art by those of ordinary skill in the art, including patent applicants, scientists, engineers and Patent Examiners.

Withdrawal of the Section 112, second paragraph, rejection of claim 34 is requested.

The Section 112, first paragraph "enablement" , rejection of claims 31, 34-48 and 50 is obviated by the above amendments. Reconsideration and withdrawal of the rejection are requested after entry of the present Amendment.

The claims define compounds wherein R₁, R₂ and R₄ are H and L₃ is a single bond. The claims therefore focus the compounds of the claims on four examples of the

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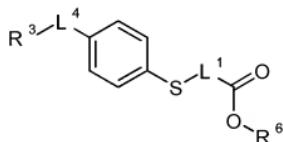
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application (i.e., compounds **A**, **E**, **iv** and **ix**), for which synthesis and biological data are specifically exemplified.

More specifically, the claims define compounds of the following structure:

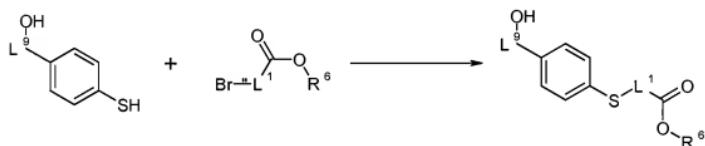


The applicants submit that one of ordinary skill in the art will be able to make and use the compounds of the claims without undue experimentation

A person ordinarily skilled in the art would not be under any undue burden to synthesize a range of compounds within the scope of the claims. The compounds covered by the claim having a core chemical structure that may be considered as a pharmacophore. This structure is a hydroxamic acid linked to a sulphur substituted aryl ring.

The variables of the claims would not require undue experimentation to synthesize, as they may be synthesized using appropriately chosen starting materials. Dorwald et al. recognizes this important factor when planning a synthetic strategy to the desired compounds in the introduction section 1.2.2.1. 'When planning a synthesis, the most suitable starting materials should be chosen.' It is clear that an ordinarily skilled organic chemist would be able to choose the appropriate starting materials when synthesizing a compound within the scope of the claims.

For example L¹ and R⁶ may be varied through the choice of bromo ester starting material. The ordinarily skilled person, as an organic chemist, would be able to apply the example reactions such as example 3, step 2 on page 52, to the reaction of any bromo ester with 4-mercaptobenzyl alcohol with reasonable expectation of success. The general reaction scheme given below is derivable directly from the application.



In addition, the coupling of a mercaptobenzyl alcohol with a bromo ester in the synthesis of two examples that fall within the scope of the current claims, A and E, is performed under the same procedure and conditions in both cases with success despite having different L¹ and R⁶ groups (see example 1, step 1 on page 49 for A, and example 3, step 2 on page 52 for E). This would indicate to the ordinarily skilled person in the art that this technique would be applicable to the formation of all variants of L¹ and R⁶.

Similarly, L⁴ and R³ may be varied by applying the synthetic procedures of the application to the appropriate starting material. The coupling of an amine to an acyl halides as for the coupling to form the hydroxyamic acid R³-L⁴ section, such as in step 3, example 1 on page 29 and step 4 of example 2 on page 53, is a well-known reaction that the person ordinarily skilled in the art would apply to a variety of amines and acyl halides.

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Reacting an amine with an acyl halide may not be the only way to achieve the hydroxamic acid group, but it is thought that the ordinarily skilled person would expect a reasonable chance of success given that acyl halides are the most reactive of acyl compounds.

The person ordinarily skilled in the art, as an organic chemist, would recognize that alternative synthetic methods may be employed to optimize the synthesis. These alternatives are readily known to the person ordinarily skilled in the art.

With regard to the Examiner's comments on the IC₅₀ data given in Table 2 of page 57, the applicants believe the same as important data for the exemplification of the efficacy of the compounds. The examples that fall within the scope of the claims show low IC₅₀ values for the inhibition of glyoxalase activity.

Data in Tables 2 and 3 are important because it clearly shows the usefulness of the four examples within the scope of the claims. Compounds A and E are active in the inhibition of glyoxalase (Table 2). The ester derivatives iv and ix are active in the cell cultures (Table 3). The data in table 3 therefore 'indicates that the ester compounds may be converted into active form in cell culture hence demonstrating their suitability for use as a prodrug compound', lines 24 to 27 on page 58.

The claims are submitted to be supported by an enabling disclosure and withdrawal of the Section 112, first paragraph "enablement", rejection is requested.

Entry of the present Amendment and allowance of all of the pending claims are requested.

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The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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